

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims: Please amend the claims as follows:

We claim:

Claim 1. (Previously Presented) A pharmaceutical composition comprising at least one agent as compound I which modulates the biological function of one or several of the VEGF/VEGF receptor systems, and further comprising at least one agent as compound II which modulates the biological function of one or several of the Angiopoietin/Tie receptor systems.

Claim 2. (Previously Presented) A pharmaceutical composition comprising at least one agent as compound I which is targeted to the endothelium via of one or several of the VEGF/VEGF receptor systems, and further comprising at least one agent as compound II which modulates the biological function of one or several of the Angiopoietin/Tie receptor systems.

Claim 3. (Cancelled)

Claim 4. (Previously Presented) A pharmaceutical composition comprising at least one agent as compound I which modulates the biological function of one or several of the VEGF/VEGF receptor systems, and further comprising at least one agent as compound II which is targeted to the endothelium via one or several of the Angiopoietin/Tie receptor systems.

Claim 5. (Previously Presented) A pharmaceutical composition comprising at least one agent as compound I which is targeted to the endothelium via one or several of the VEGF/VEGF receptor systems, and further comprising at least one agent as compound II which is targeted to the endothelium via one or several of the Angiopoietin/Tie receptor systems.

Claim 6. (Previously Presented) A pharmaceutical composition

comprising at least one agent as compound I which modulates the biological function of one or several of the VEGF/VEGF receptor systems, and further comprising at least one agent as compound II which is targeted to the endothelium via one or several of the VEGF/VEGF receptor systems.

Claim 7. (Previously Presented) A pharmaceutical composition comprising at least one agent as compound I which modulates the biological function of one or several of the Angiotensin/Tie receptor systems, and further comprising at least one agent as compound II which is targeted to the endothelium via one or several of the Angiotensin/Tie receptor systems.

Claim 8. (Withdrawn) Pharmaceutical compositions comprising one or several agents which interfere with both the function of one or several of the VEGF/VEGF receptor systems and the function of one or several of the Angiotensin/Tie receptor systems.

Claim 9. (Previously Presented) A pharmaceutical composition according to claim 1 which is adopted for simultaneous or separate sequential therapeutic application.

Claim 10. (Previously Presented) A pharmaceutical composition according to claim 1 which comprises as compound I at least one of

- a) a compound which inhibits receptor tyrosine kinase activity,
- b) a compound which inhibits ligand binding to receptors,
- c) a compound which inhibits activation of intracellular signal pathways of the receptors,
- d) a compound which inhibits or activates expression of a ligand or of a receptor of the VEGF or Tie receptor system,
- e) a delivery system comprising an antibody, a ligand, a high-affinity binding oligonucleotide or oligopeptide, or a liposome, which targets cytotoxic agents or coagulation-inducing agents to the endothelium via recognition of VEGF/VEGF receptor or Angiotensin/Tie receptor systems,
- f) a delivery system comprising an antibody, a ligand, a high-affinity binding

oligonucleotide or oligopeptide, or a liposome, which is targeted to the endothelium and induce necrosis or apoptosis.

Claim 11. (Previously Presented) A pharmaceutical composition according to claim 1 which comprises as compound II at least one of

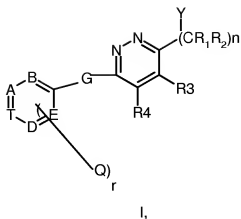
- f) a compound which inhibits receptor tyrosine kinase activity,
- g) a compound which inhibits ligand binding to receptors,
- h) a compound which inhibits activation of intracellular signal pathways of the receptors,
- i) a compound which inhibits or activates expression of a ligand or of a receptor of the VEGF or Tie receptor system,
- j) a delivery system comprising an antibody, a ligand, a high-affinity binding oligonucleotide or oligopeptide, or a liposome, which targets cytotoxic agents or coagulation-inducing agents to the endothelium via recognition of VEGF/VEGF receptor or Angiopoietin/Tie receptor systems,
- k) a delivery system comprising an antibody, a ligand, a high-affinity binding oligonucleotide or oligopeptide, or a liposome, which is targeted to the endothelium and induce necrosis or apoptosis.

Claim 12. (Withdrawn) Pharmaceutical compositions according to claim 1 which comprise as compound I and/or II at least one of Seq. ID Nos. 1-59.

Claim 13. (Withdrawn) Pharmaceutical compositions according to claim 1 which comprise as compound I and/or II SEQ ID NO:60.

Claim 14. (Withdrawn, Currently Amended) ~~Pharmaceutical—compositions~~ A pharmaceutical composition according to claim 1 which comprise as compound I and/or II at least one of sTie2, mAB 4301-42-35, scFv-TTF and/ or L19 scFv-TTFconjugate.

Claim 15. (Withdrawn, Currently Amended) ~~Pharmaceutical—compositions~~ A pharmaceutical composition according to claim 1 which comprise as compound I and/ or II at least one small molecule of ~~general formula I~~ general formula I



in which

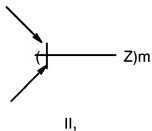
r has the meaning of 0 to 2,

n has the meaning of 0 to 2;

R₃ und R₄

a) each independently from each other have the meaning of lower alkyl,

b) together form a bridge of general partial formula II,



wherein the binding is via the two terminal C- atoms,

and

m has the meaning of 0 to 4; or

c) together form a bridge of partial formula III



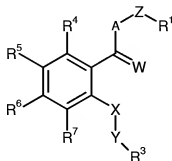
wherein one or two of the ring members T₁, T₂, T₃, T₄ has the meaning of nitrogen, and each others have the meaning of CH, and the binding is via the atoms T₁ and T₄;

- G has the meaning of C₁ - C₆ - alkyl, C₂ - C₆ - alkylene or C₂ - C₆ - alkenylene; or C₂ - C₆ - alkylene or C₃ - C₆ - alkenylene, which are substituted with acyloxy or hydroxy; -CH₂-O-, -CH₂-S-, -CH₂-NH-, -CH₂-O-CH₂-, -CH₂-S-CH₂-, -CH₂-NH-CH₂-, oxa (-O-), thia (-S-) or imino (-NH-),
- A, B, D, E and T independently from each other have the meaning of N or CH, with the proviso that not more than three of these Substituents have the meaning of N,
- Q has the meaning of lower alkyl, lower alkyloxy or halogene,
- R₁ and R₂ independently from each other have the meaning of H or lower alkyl,
- X has the meaning of imino, oxa or thia;
- Y has the meaning of hydrogen, unsubstituted or substituted aryl, heteroaryl, or unsubstituted or substituted cycloalkyl; and
- Z has the meaning of amino, mono- or disubstituted amino, halogen, alkyl, substituted alkyl, hydroxy, etherificated or esterificated hydroxy, nitro, cyano, carboxy, esterificated carboxy, alkanoyl, carbamoyl, N-mono- or N, N-disubstituted carbamoyl, amidino, guanidino, mercapto, sulfo, phenylthio, phenyl-lower-alkyl-thio, alkyl-phenyl-thio, phenylsulfanyl, phenyl-lower-alkyl-sulfanyl, alkylphenylsulfanyl, phenylsulfonyl, phenyl-lower-alkyl-sulfonyl, or alkylphenylsulfonyl,

whereas, if more than one rest Z is present (m>2), the substituents Z are equal or different from each other,

and

wherein the bonds marked with an arrow are single or double bonds; or an N-oxide of said compound, wherein one or more N-atoms carry an oxygen atom, or a salt thereof,
and/or a compound of general formula IV



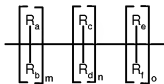
IV

in which

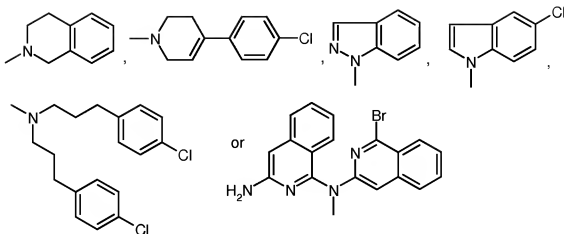
A has the meaning of group $=NR^2$,

W has the meaning of oxygen, sulfur, two hydrogen atoms or the group $=NR^8$,

Z has the meaning of the group $=NR^{10}$ or $=N-$, $-N(R^{10})-(CH_2)_q-$, branched or unbranched C_{1-6} -Alkyl or is the group



or A, Z and R^1 together form the group



m, n and o

has the meaning of 0 – 3,

q

has the meaning of 1 – 6,

R_a, R_b, R_c, R_d, R_e, R_f

independently from each other have the meaning of hydrogen, C₁₋₄ alkyl or the group =NR¹⁰, and/ or R_a and/ or R_b together with R_c and or R_d or R_c together with R_e and/ or R_f form a bound, or up to two of the groups R_a-R_f form a bridge with each up to 3 C-atoms with R¹ or R²,

X

has the meaning of group =NR⁹ or =N-,

Y

has the meaning of group -(CH₂)_p,

p

has the meaning of integer 1-4,

R¹

has the meaning of unsubstituted or optionally substituted with one or more of halogene, C₁₋₆-alkyl, or C₁₋₆-alkyl or C₁₋₆-alkoxy, which is optionally substituted by one or more of halogen, or is unsubstituted or substituted aryl or heteroaryl,

R²

has the meaning of hydrogen or C₁₋₆-alkyl, or form a bridge with up to 3 ring atoms with R_a-R_f together with Z or R₁,

R³

has the meaning of monocyclic or bicyclic aryl or heteroaryl which is unsubstituted or optionally substituted with one or more of fur halogen, C₁₋₆-alkyl, C₁₋₆-alkoxy or hydroxy,

R⁴, R⁵, R⁶ and R⁷

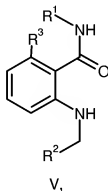
independently from each other have the meaning of

hydrogen, halogene or C₁₋₆-alkoxy, C₁₋₆-alkyl or C₁₋₆-carboxyalkyl, which are unsubstituted or optionally substituted with one or more of halogene, or R⁵ and R⁶ together form the group



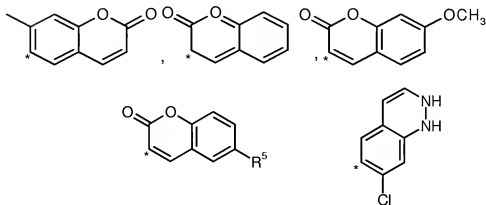
R⁸, R⁹ and R¹⁰ independently from each other have the meaning of hydrogen or C₁₋₆-alkyl, as well as their isomers and salts,

and/ or a compound of general formula V

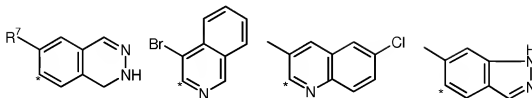


in which

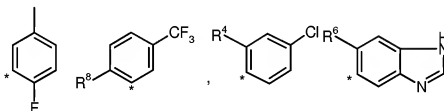
R¹ has the meaning of group



in which R⁵ is chloro, bromo or the group -OCH₃,



in which R⁷ is -CH₃ or chloro,

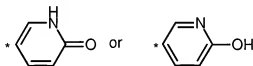


in which R⁸ is -CH₃, fluoro, chloro, or -CF₃,

in which R⁴ is fluoro, chloro, bromo, -CF₃, -N=C, -CH₃, -OCF₃ or -CH₂OH

in which R⁶ is -CH₃ or chloro

R² has the meaning of pyridyl or the group



and

R³ has the meaning of hydrogen or fluoro,

as well as their isomers and salts.

Claim 16. (Withdrawn, Currently Amended) ~~Pharmaceutical~~ compositions A pharmaceutical composition according to claim 15 which comprise as compound I and/or II (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate.

Claim 17. (Withdrawn, Currently Amended) Pharmaceutical—compositions A pharmaceutical composition according to claim 1 which comprise as compound I (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate, sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTF conjugate, and as compound II (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate, sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTF conjugate, with the provision that compound I is not identically to compound II.

Claim 18. (Withdrawn, Currently Amended) Pharmaceutical—compositions A pharmaceutical composition according to claim 1 which comprise as compound I (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate and as compound II sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTF conjugate.

Claim 19. (Withdrawn, Currently Amended) Pharmaceutical—compositions A pharmaceutical composition according to claim 1 which comprise as compound I mAB 4301-42-35 and as compound II sTie2, and/ or scFv-tTF conjugate.

Claim 20. (Withdrawn, Currently Amended) Pharmaceutical—compositions A pharmaceutical composition according to claim 1 which comprise as compound I scFv-tTF conjugate and as compound II sTie2 and/ or mAB 4301-42-35.

Claim 21. (Withdrawn, Currently Amended) Pharmaceutical—compositions A pharmaceutical composition according to claim 1 which comprise as compound I L19 scFv-tTF conjugate and as compound II sTie2.

Claim 22. (Withdrawn, Currently Amended) Use of pharmaceutical compositions according to claim 1, for the production of a medicament for the treatment of A method of treating tumors, cancers, psoriasis, arthritis, such as rheumatoid arthritis, hemangioma, angiofibroma, eye diseases, such as diabetic retinopathy, neovascular glaucoma, kidney diseases, such as glomerulonephritis, diabetic nephropathy, malignant nephrosclerosis, thrombotic microangiopathic syndrome, transplantation rejections, and glomerulopathy, fibrotic diseases, such as cirrhotic liver, mesangial cell

proliferative diseases, ~~arteriosclerosis~~ arteriosclerosis, damage of nerve tissues, or for the suppression of the ascites formation in patients and or for the suppression of VEGF oedemas in a subject, comprising administering into said subject an effective amount of the pharmaceutical composition of claim 1.

Claim 23. (New) A method of treating a tumor or tumor metastasis in a subject, comprising administering into said subject an effective amount of the pharmaceutical composition of claim 1.

Claim 24. (New) The pharmaceutical composition of claim 1 wherein compound I is 4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate and compound II is sTie2.